

OBSERVATIONS
AND
EXPERIMENTS ON PERUVIAN BARK.

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THE cinchona, or as it is more generally denominated, Peruvian Bark, is the product of several species of the genus *Cinchona*, which in botanical arrangement, belongs to the class Pentandria, order Monogynia, and to the natural order Contorta.

The descriptions of the species of this genus, from the limited and imperfect nature of the information possessed, have been generally so confused and indefinite, as to convey little or no information.

Cinchona is found in various parts of South America, always inhabiting mountainous tracts, where it grows from a few inches in diameter to the thickness of a man's body. The bark is collected in the dry season, say from September till November, and after being well dried in the sun, is packed up in skins, forming what is called *seroons*, weighing from fifty to one hundred and fifty pounds.

Several species are frequently mixed together in these seroons, which are afterwards separated, according to quality: it is not, however, uncommon to find several species mixed together on their arrival at our markets. The tree has never yet been cultivated by the Spaniards, who procure it by stripping the natural trees of their bark, which ultimately must destroy the genus, as they always die after the operation.

Most of the varieties of cinchona being highly valuable, and consequently very liable to be adulterated with various substances, it is therefore important to adhere to a critical examination of all its characters.

The accounts of the discovery of cinchona are very numerous, and many from their singularity and improbability,

are no doubt founded in fiction. It has long been esteemed a valuable medicine in Peru, where it is said the natives have adopted its use, from observing that animals recur to it. Be the source of its first employment what it may, it was not used by Europeans until the year 1640, when the countess Cinchon, wife of the Spanish viceroy, was cured of the ague by means of it, and hence the derivation of its name, cinchona. As frequently occurs on the introduction of any *new remedy*, considerable noise was made, and opposition raised against it by several eminent physicians; but when submitted to proper experiments, its efficacy soon suppressed the groundless clamor which had been too hastily excited.

The principle, says Dr. Paris, on which the tonic and febrifuge properties of bark depend, has ever been a fruitful source of controversy. Deschamps attributed it to cinchonate of lime. Westering considered tannin as the active principle; while M. Seguin assigned all the virtues to the principle which precipitates gallic acid. Fabroni concluded from his experiments, that the febrifuge power of the bark did not belong exclusively and essentially to the astringent, bitter, or to any other individual principle; since the quantity of these would necessarily be increased by long boiling; whereas the virtues of the bark are notoriously diminished by protracted ebullition.

Perhaps no vegetable substance, underwent so many analyses, by the most distinguished chemists of Europe, as the cinchona; and yet so little positive knowledge was obtained of its true constituents, and such was the very obscure condition of our information of the active principle of cinchona, when the scrutinizing, critical and successful researches of Pelletier and Caventou, detected the existence of two salifiable bases, in peculiar states of combination, in the different species of cinchona. The medical profession is therefore indebted to these intelligent and enterprising chemists, for one of the most valuable additions ever made to the *materia medica*.

Among all the late discoveries in vegetable chemistry, there is none which claims so much attention from extensive usefulness, as that of quinine. This principle contains all the tonic and febrifuge properties of Peruvian bark, in their most concentrated state. By the substitution of this preparation for the crude bark, the physician can conveniently administer it to the most delicate constitution, in an eligible form,

and by no means an unpleasant dose, what previously was considered the most nauseous and disagreeable medicine, and frequently, from its bulky nature, (when administered in less than ordinary doses,) was rejected by the stomach.

In consequence of the prevailing endemics, ague and remittent fevers, which of late years have visited almost every section of our country, the article *cinchona* has increased very much in practice and demand, and become one of the most important articles of the *materia medica*.

The descriptions which have been given by most authors, to distinguish the many species and varieties of this extensive and important genus, are so imperfect and confused, that they tend rather to involve research in more dense obscurity, than to develop any information. It is admitted, there is no method so well calculated to ascertain, with any degree of certainty, the comparative activity of the different species of Peruvian bark, as that of analysis; and from this circumstance, I have made trial of some of the most important species, which now occur in our commerce, for the purpose of determining their qualities; which I have done by extracting the alkaline principle, upon which their virtue as a medicine entirely depends, and from the product of which, their comparative strength may be accurately and readily ascertained.

It is a source of regret, that many of our country physicians so little appreciate the quality of *cinchona*, as to be governed entirely by the price, which from the following statement, will appear to be the most remote and inaccurate grounds for calculation, as the cheapest or lowest priced bark in the market, is far dearer to the practitioner, and particularly to the patient, than that which commands the highest price; for it not only requires the patient to swallow twelve times the quantity to produce the same effect, independent of the loss of time, but also by charging the stomach, when in a weak and debilitated state, with so large a portion of ligneous and insoluble matter, may give rise to diseases more serious than those for which it was administered as a remedy.

The bark of commerce, in this country and in England, is generally designated under the limited nomenclature of red, pale and yellow. There are now no less than twenty five distinct species of *cinchona*, independent of any additions we may owe to the zeal of Humboldt and Bonpland, as well as of Mr. A. T. Thompson, who states, that in a large collection

of dried specimens of the genus *cinchona* in his possession, collected in 1805, both near Loxa and Santa Fé, he finds many specimens which are not mentioned in the works of any Spanish botanist.

Dr. Paris, in his valuable *Pharmacologia*, justly remarks, that notwithstanding the labors of the *Spanish botanists*, the history of this important genus is still involved in considerable perplexity; and owing to the mixture of the barks of several species, and their importation into Europe under one common name, it is extremely difficult to reconcile the contradictory opinions which exist upon this subject. Under the trivial name *officinalis*, Linnæus confounded no less than four distinct species of *cinchona*; and under the same denomination, the British Pharmacopœias for a long period placed as varieties, the three barks known in the shops: this error indeed is still maintained in the Dublin Pharmacopœia, but the London and Edinburgh colleges, have at length adopted the arrangement of Mutis, a celebrated botanist who has resided in South America, and held the official situation of director of the importation of bark for nearly forty years.

The apothecaries of this country and England, at the present day, distinguish the denomination of their bark, by terms expressive of the color; and it is a source of still greater surprise, to find the orders and prescriptions of some of our most intelligent physicians, designating the species of bark they wish to employ, by no other than one of the terms signifying red, pale or yellow: thus reducing the extensive genus *cinchona*, of not less than twenty five species into three varieties, and leaving it entirely to the discretion of the apothecary, to give him any species, of a color correspondent to that ordered. Independent of the great insufficiency of these terms to distinguish the numerous species, the color of the powder, is one of the most uncertain and inaccurate methods which could be adopted, of classing or assorting the *cinchonas*; as under the same denomination, the best species of bark in commerce, (*calisaya arrollenda*), would be confounded with the most inferior, (*carthagena*), as the color of the powders of both is yellow; hence a physician writing for yellow bark, leaves it to the choice of the apothecary, to give him what species he may think proper, of a correspondent color, but varying in quality from *calisaya* to *carthagena*, or in medicinal activity as from 12 to 1.

The importance therefore of adopting terms more definite to distinguish the several species of Peruvian bark must be obvious, and that the botanical nomenclature of these species is imperfect and inadequate, is equally so. The quality of Peruvian bark appears to be modified and influenced by locality, produced by difference in soil, altitude of situation, exposure, or some other circumstances peculiar to the location, hence the different provinces of Peru afford bark differing very materially in their physical characters and particularly in the activity of their medical qualities, from which circumstances it would appear that a nomenclature derived from the names of the provinces in which the different species grow, would be a systematic arrangement.

The following are some of the most important species which now occur in commerce which I have submitted to experiments, and have given to each the comparative proportion of quinine and cinchonine which they respectively contain. The names which are given to distinguish these several species, are derived from the provinces in which they grow, which at present, (in consequence of the confusion in the botanical history and arrangement of cinchona,) is the most direct and certain mode of distinguishing those species of bark which now are found in our shops.

Calisaya Bark—Two Varieties.

Of this very important species there are two varieties in commerce.

1st. *Calisaya arrollenda*, (Quill *Calisaya*.) This variety is in quills from three quarters of an inch to an inch and a half in diameter, and from eight inches to a foot and a half in length. The epidermis is thick and may be readily removed from the bark; and hence you find in the seroons or cases a great proportion deprived of this inert part. It is generally imported in seroons weighing about one hundred and fifty pounds, and very seldom comes in cases; it has many deep transversal fissures running parallel, the fracture is woody and shining, the interior layer is fibrous and of a yellow color, and the taste is slightly astringent and very bitter.

This species of bark will yield a much larger proportion of the active principle, (quinine,) than any other bark in commerce, and consequently may be justly esteemed the best.

2nd. *Calisaya Plancha*, (Flat *Calisaya*.) This variety consists of flat, thick, woody pieces, of a reddish brown colour, deprived of its epidermis, and the interior layer more fibrous than that in the quill. This variety yields from twenty to twenty-five per cent less quinine than the *arrollenda*, and is consequently a less desirable article.

Superior Loxa or Crown Bark.

Loxa is the name of the province and port, where this bark is obtained and from which it is exported. In this province *cinchona* was originally discovered. This bark has been highly esteemed by the royal family, and is that which has been selected for their use; hence, the name of *Crown Bark*. The following are the characters which distinguish this bark.

The *Loxa* bark occurs in small quills, the longitudinal edges folding in upon themselves forming a tube about the circumference of a goose quill, and from half a foot to a foot and a half in length. It is of a greyish colour on the exterior, and covered with small transverse fissures or cracks, the interior surface is smooth and in fresh or good bark of a bright orange red, it is of a compact texture and breaks with a short clear fracture, it is the bark of the *cinchona condaminia* and is known at *Loxa* by the name of *cascarilla fina*. Yet, notwithstanding this bark appears to have held the decided preference to all other species, analysis fully indicates that it is not equal in medicinal strength by at least twenty-five per cent, to that denominated *Calisaya*; this bark is more astringent and less bitter than the *calisaya*.

This species yields from twenty-five to thirty per cent, less cinchonine and quinine, than the *caylisaya arrollenda* does quinine, and the proportion of cinchonine is much greater than that of the quinine.

Cinchona Oblongifolia or Red Bark.

The above term appears to be more applicable to the species in question, than any other which can be selected, as under that denomination the best red bark has always been well known, and as there is but one other species affording a red powder, it is not likely to be confounded. The inferior red bark of which there is a considerable quantity in our

market, is no doubt more frequently obtained by colouring low priced yellow bark, than from the product of a distinct species.

There is but one species of bark in addition to the *Oblongifolia* as before stated, producing a red powder which is called *Rosea*, and as that species is seldom or never known in our commerce there can be little or no powder produced by it, hence, all the inferior kinds of red bark of which there is no small quantity to the discredit of those who sell it, evidently must be either such of the *Oblongifolia* as has been rendered almost inactive, by age, weather, or some other exposure, or as before surmised, is inferior yellow bark, coloured, and as the product of the former must be small, it in all probability proceeds from the latter source; hence the price of red bark is as various, (and the *qualities* corresponding with the prices,) as the yellow bark, although the number of species of which we are acquainted is not one eighth the number of the latter.

The *cinchona oblongifolia* is the *magnifolia* of the flora Peruviana, and is known in Spain by the name of *Colorada*, and is what constitutes the red bark of commerce; it occurs generally in large thick pieces, being the product of the largest tree of the genus *cinchona oblongifolia*. There are two varieties.

1st. *Colorada Canan*, or *Quill Red Bark* which occurs in quills of various diameters, from one fourth of an inch to two inches in thickness. The epidermis is white or grey, with transversal fissures or warty concretions of a reddish color, the interior is of a brick red color, the cross fracture short and fibrous, the longitudinal fracture compact and shining, the taste not so bitter as that of the *calisaya*.

2nd. *Colorada Plancha*, or *Flat Red Bark*. This bark is in very large thick pieces, from half an inch to two inches in thickness, and from one to two feet in length, the epidermis brown, thick and rugged with cracks running in various directions. The fracture very fibrous inside, is of a deep brick color, the taste is less bitter than that of the quill, and of course much less so than that of the *calisaya*.

These two varieties frequently come in the same seroon, and from their appearance are no doubt the product of the same species, or perhaps the same tree; the quill being produced by the branches and the flat thick pieces from the trunk, or the former from young and the latter from older trees.

This bark is generally more scarce in our market than the yellow or pale, and commands a higher price : within a short period however, about fifty seroons of this bark have been imported from Guayaquil by Mr. John R. Neff, which has in a small degree influenced the price of the article. I am informed by a respectable druggist of this city, who has been a long time established in business, that this is the only arrival in quantity, of red bark, direct from South America within his recollection, the supplies heretofore having been received from Europe. These seroons averaged about one hundred pounds each. The bark was very fresh and of a very superior quality. The large flat pieces and quills were indiscriminately mixed and in some seroons in very nearly equal proportions. This bark when first received, was of a very deep and bright color, and particularly the powder produced by the flat pieces ; after being exposed however, in a dry place for about six months, it faded considerably, insomuch that any one not in possession of the proof of the fact, would have doubted, whether the powder had been produced from the same bark.

From experiments on the above bark, I procured twenty per cent less cinchonine and quinine, taken together, than the amount of quinine produced by the same quantity of calisaya arrollenda bark ; and the proportion of cinchonine, was rather more than half of the product of quinine.

It will appear therefore, from what has been said, that notwithstanding the great prejudices, both of eminent authors and skilful practitioners, which have so long existed in favor of the superiority of the *oblongifolia*, (red bark,) over other species ; that it is decidedly inferior to the *calisaya*, (yellow bark,) as the whole product, as before stated, of its active principles, does not equal that of the calisaya and cinchonine, constituting rather more than half the product, which, according to an eminent author, is five times less active than the quinine ; this point however, I think is very far from being settled. An interesting paper was read before the Academy of Medicine, at Paris, which is published in the Bulletin des Sciences Medicales, for November, 1825, in which M. Bally states that he has experimented upon the sulphate of cinchonine, with a view to determine its febrifuge qualities. He administered this sulphate in twenty seven cases of intermittent fevers, of different types, in doses of two grain pills, giving three or four in the interval of par-

oxysms; by which treatment he cured the disease as effectually and as speedily as with the quinine: of which twenty seven cases, there were sixteen tertian, nine quotidian and two quartan. He remarked further, that the cinchonine has properties less irritating than those of quinine, and that consequently its employment should be more general, and preferred in all simple cases. I believe few or no experiments have been made by the physicians of this country, upon the medical properties of the cinchonine; it consequently must be very little known by them from their own experience, but it certainly is a medicine which deserves at least a trial.

From the preceding description, the several species of Peruvian bark most commonly met with at the present day, may be readily recognised, as the physical characters are prominent and distinctive in each variety; after however selecting the best species of Peruvian bark, by the several distinguishing and specific characters, one very important adventitious condition yet remains to be investigated. It is a fact established beyond controversy, that age is a very powerful agent in deteriorating the active properties of bark, inasmuch that the best species of Peruvian bark when old, is little superior and sometimes even inferior to the carthagena bark when fresh; hence it is, that large parcels of a superior species of Peruvian bark, which would have commanded two dollars per pound at Cadiz, when fresh, has been offered publicly in this city for one-eighth the sum, twenty five cents, and that without a purchaser; and which it appears has been operated upon by no other unfavorable circumstance but age. In what manner or by what process age, or rather the circumstances connected with it, act upon bark other than by a combination with oxygen or a volatilization of its active principle, I know not. Fabroni states with truth, that cinchona loses its solubility, and consequently its activity, by long exposure to the air, but does not give his opinion as to the manner in which it is thus affected. I cannot, however, conceive under existing circumstances, how the solubility of Peruvian bark can be diminished, except through the agency of oxygen, and it is by this means the extract of bark, prepared according to the common formulas of our dispensaries, is rendered devoid of utility; for owing to the oxygenization of the extractive matter, the solubility of the extract is so diminished during its formation, that scarcely one half is soluble in water.

From a number of experiments which I have made upon Peruvian bark in different states, I have observed as an unequivocal result, that the same species of bark which when fresh is very productive of quinine, when old will produce little or none of this active principle, upon which its virtue as a medicine entirely depends.

It will appear therefore an important duty, critically to examine the state of bark as to age, and it may perhaps be useful in this place, to describe the physical characters of bark in this state, and by which it may be readily known. The prominent features which characterize old bark, and distinguish it from recent, are the following. Old bark has lost nearly all that bitter and astringent taste and peculiar aromatic odor, which are such prominent characteristics of recent bark of good quality. The specific gravity is also sensibly diminished, and the fracture instead of being shining and compact is dull, fibrous and of a loose texture, and the color very frequently passes from a bright orange to a dull brown, as the bark advances in age, particularly if much exposed. By attention to these few conspicuous characters, taste, smell, specific gravity, fracture and color, no mistake can arise in the selection of good bark, unless there is a gross deficiency of judgment. Yet notwithstanding the distinguishing characters of Peruvian bark in these two states are so prominent and striking, we regret to say, that gross mistakes have been made public in this particular, by men whom we might suppose most capable of appreciating the quality, under the influence of every incidental circumstance.

Dr. Paris in the sixth edition of his *Pharmacologia*, makes the following remarks under the article *cinchona*. The frauds committed under this head are most extensive; it is not only mixed with inferior bark, but frequently with genuine bark, the active constituents of which have been extracted by decoction with water. In selecting *cinchona* bark, the following precautions may be useful; it should be dense, heavy and dry, not musty, nor spoiled by moisture; a decoction made of it should have a reddish color when warm, but when cold it should become paler, and deposit a brownish red sediment. When the bark is of a dark color, between red and yellow, it is either of a bad species or it has not been well preserved. Its taste should be bitter, with a slight acidity, but not nauseous nor very astringent; when chewed, it should not appear in threads nor of much length, the odour

is not very strong, but when bark is well cured it is always perceptible, and the stronger it is, provided it be pleasant, the better may the bark be considered. In order to give bark the form of quill, the bark gatherers not unfrequently call in the aid of artificial heat, by which its virtues are deteriorated, the fraud is detected by the colour being much darker, and upon splitting the bark, by the inside exhibiting stripes of a whitish sickly hue. In the form of powder, cinchona is always found more or less adulterated. *This must be recollected as applying to the English market.* During a late official inspection of the shops of apothecaries and druggists, the censors repeatedly met with powdered cinchona having a hard metallic taste, quite foreign to that which characterizes good bark.* The best test of the goodness of bark, is afforded by the quantity of cinchona or quina that may be extracted from it; and the manufacturer should always institute such a trial before he purchases any quantity, taking a certain number of pieces indiscriminately from the bulk.

Before concluding, it may not be out of season to remark, that the sulphate of quinine, as it is generally termed, is not a perfectly neutral salt, but in the state of a sub-sulphate, and is only partly soluble in water. Its exhibition in water is rendered much more eligible by the addition of a drop of sulphuric acid to each grain of the salt, which makes a perfectly transparent solution, and which, I think, from its obvious advantages, should entirely supercede the common formula: with sugar and gum arabic, a few grains of citric or tartaric acid will have the same effect in dissolving the quinine as the sulphuric acid, and has been preferred by some.

Dr. Paris,† on the exhibition of quinine, states that he lately saw a prescription in which the salt is directed to be rubbed with a few grains of cream of tartar, and then to be dissolved in mint water. This, he continues, is obviously injudicious, since tartaric acid decomposes the sulphate, and occasions an insoluble tartrate which is precipitated.

* Mr. Thompson has suggested the probability of this circumstance having arisen from the admixture of a species of bark, lately introduced into Europe from Martinique, resembling the *cinchona floribunda*, and which by an analysis of M. Cadet was found to contain iron.—*London Disp. Edit.* 3, p. 247.

† Pharmacologia, Edit. 6, vol. ii, p. 163.

With due deference to the exalted judgment of Dr. Paris, I must however, on the following grounds, dissent from his opinions. The cream of tartar is objectional, merely from the circumstance that the active part of the compound may be obtained in a more direct and speedy process by the tartaric acid. The combination of cream of tartar and sulphate of quinine in the above prescription, does produce decomposition as Dr. Paris has observed, but the virtue of the medicine is not in the least affected by it, and the precipitate, instead of being an insoluble tartrate of quinine as he observes, is sulphate of potass; tartrate of quinine is a very soluble salt, and is held in solution while the water becomes slightly turbid by the precipitation of sulphate of potass, which, however from its extremely minute division is speedily taken up by the water, when you have a transparent solution of tartrate of quinine and sulphate of potass, and as the latter answers neither a good nor a bad purpose, it of course can very conveniently be dispensed with, and therefore, as before stated, the tartaric acid should be preferred as having a more speedy and direct action.

Piperine has proved a valuable adjunct to quinine; equal proportions of each will act with much more energy than the whole quantity of quinine or piperine alone. Dr. Chapman informs us, he has met with much success in the treatment of intermittent fevers by employing the following prescription.

R Quinine grs ×
 Piperine grs ×
 M. ft. Pill No ×

One to be taken every hour in the absence of fever.

Oil of black pepper is much more active than piperine, one drop being fully equal to three grains of piperine, three drops of oil of black pepper added to ten grains of quinine, will greatly increase the powers of this remedy, oil of black pepper alone is a valuable stimulant in typhus fever, and is a valuable adjunct to many medicines.

All the preceding varieties of bark, sulphate of quinine, cinchonine, and all the preparations of bark and quinine, may be procured at Geo. W. Carpenter's Chemical Warehouse, 301 Market street, Philadelphia.

Note.—An alkaline substance somewhat analagous to quinine, has recently been discovered in the cornus florida,

which has been denominated cornine, and which has been very carefully and accurately described by Dr. Samuel G. Morton in the Philadelphia Journal of Medical and Physical Sciences. From the most respectable sources in the medical profession, from various parts of the United States where the article has been sent, the most favourable accounts have been received of the unequivocal success of the cornine in the treatment of intermittent fevers in the same doses as the quinine, and the only circumstance which precludes its competition with that substance, is the extremely minute comparative proportion of cornine yielded by the cornus florida.